

What is claimed is:

1. An oligonucleotide having a sequence complementary to a sequence of a ribonucleic acid encoding a heparanase, wherein:
  - (a) the oligonucleotide hybridizes with the ribonucleic acid under conditions of high stringency and is between 10 and 40 nucleotides in length;
  - (b) the internucleoside linkages of the oligonucleotide comprise at least one phosphorothioate linkage; and
  - (c) hybridization of the oligonucleotide to the ribonucleic acid inhibits expression of the heparanase, wherein inhibition of heparanase expression means at least a 50% reduction in the quantity of heparanase as follows: (a) a T24 bladder carcinoma cell is exposed to a complex of the oligonucleotide and lipofectin at an oligonucleotide concentration of 1  $\mu$ M and a lipofectin concentration of 10  $\mu$ g/ml for 5 hours at 37°C, (b) the complex is completely removed after such exposure, (c) 19 hours later the cell is scraped, washed and extracted in lysis buffer, (d) the nucleus of the cell is removed by centrifugation, (e) the cytoplasmic proteins in the resulting supernatant are separated according to mass by sodium dodecyl sulphate polyacrylamide gel electrophoresis, (f) the protein is transferred to a polyvinylidene difluoride membrane that is incubated at room temperature for 1-2 hours in incubation solution (g) the

membrane is exposed to 1 µg/ml of an antibody directed against heparanase at 4°C for 12 hours, (h) the membrane is exposed to wash buffer and incubated for 1 hour at room temperature in blocking buffer comprising a 1:3,000 dilution of a peroxidase-conjugated secondary antibody directed against an epitope on the antibody directed against heparanase, (i) the membrane is exposed to a chemiluminescent cyclic diacylthydrazide and the oxidation of the cyclic diacylthydrazide by the peroxidase is detected as a chemiluminescent signal, and (j) the signal is quantitated by laser-scanning densitometry as a measure of the amount of heparanase expressed calculated as a percentage of heparanase expression in an untreated cell.

2. The oligonucleotide of claim 1, wherein the oligonucleotide comprises deoxyribonucleotides.
3. The oligonucleotide of claim 1, wherein the oligonucleotide comprises ribonucleotides.
4. The oligonucleotide of claim 1, wherein every internucleoside linkage is a phosphorothioate linkage.
5. The oligonucleotide of claim 1, wherein the oligonucleotide is between 15 and 25 nucleotides in length.
6. The oligonucleotide of claim 1, wherein the oligonucleotide is about 20 nucleotides in length.

7. The oligonucleotide of claim 1, wherein the sequence of the oligonucleotide is selected from the following:

- 5           (a) CCCCAGGAGCAGCAGCAGCA (SEQ ID NO:3);  
            (b) GTCCAGGAGCAACTGAGCAT (SEQ ID NO:4); and  
            (c) AGGTGGACTTTCTTAGAAGT (SEQ ID NO:5).

10           8. The oligonucleotide of claim 1, wherein the oligonucleotide further comprises a modified internucleoside linkage.

15           9. The oligonucleotide of claim 8, wherein the modified internucleoside linkage is a peptide-nucleic acid linkage, a morpholino linkage, a phosphodiester linkage or a stereo-regular phosphorothioate.

20           10. The oligonucleotide of claim 1, wherein the oligonucleotide further comprises a modified sugar moiety.

11. The oligonucleotide of claim 10, wherein the modified sugar moiety is 2'-O-alkyl oligoribonucleotide.

25           12. The oligonucleotide of claim 1, wherein the oligonucleotide further comprises a modified nucleobase.

30           13. The oligonucleotide of claim 12, wherein the modified nucleobase is a 5-methyl pyrimidine or a 5-propynyl pyrimidine.

14. The oligonucleotide of claim 1, wherein the heparanase is a human heparanase.

5 15. A method of inhibiting expression of a heparanase in a cell comprising contacting the cell with the oligonucleotide of claim 1 under conditions such that the oligonucleotide hybridizes with mRNA encoding the heparanase so as to thereby inhibit the expression of the heparanase.

10 16. The method of claim 15, wherein the cell is a cancer cell.

15 17. A composition comprising the oligonucleotide of claim 1 in an amount effective to inhibit expression of a heparanase in a cell and a carrier.

20 18. The composition of claim 17, wherein the oligonucleotide and the carrier are capable of passing through a cell membrane.

19. The composition of claim 18, wherein the carrier comprises a membrane-permeable cationic reagent.

25 20. The composition of claim 19, wherein the cationic reagent is lipofectin.

30 21. A method of treating a tumor in a subject which comprises administering to the subject an amount of the oligonucleotide of claim 1 effective to inhibit expression of a heparanase in the subject and thereby treat the tumor.

22. A method of treating a subject which comprises administering to the subject an amount of the oligonucleotide of claim 1 effective to inhibit expression of a heparanase in the subject and thereby treat the subject.
23. The method of claim 21 or 22, wherein the subject is a human being.
24. The method of claim 21, wherein the treatment of the tumor is effected by reducing tumor growth.
25. The method of claim 21, wherein the treatment of the tumor is effected by reducing tumor metastasis.
26. The method of claim 21, wherein the treatment of the tumor is effected by reducing angiogenesis.
27. Use of the oligonucleotide of claim 1 for the preparation of a pharmaceutical composition for treating a tumor in a subject which comprises admixing the oligonucleotide in an amount effective to inhibit expression of a heparanase in the subject, with a pharmaceutical carrier.
28. An oligonucleotide having a sequence complementary to a sequence of a ribonucleic acid encoding a heparanase, wherein:
- (a) the oligonucleotide hybridizes with the ribonucleic acid under conditions of high stringency and is between 10 and 40 nucleotides

in length;

(b) the internucleoside linkages of the oligonucleotide comprise at least one phosphorothioate linkage; and

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(c) hybridization of the oligonucleotide to the ribonucleic acid inhibits expression of the heparanase.

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